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10/541,068	05/15/2006	Jens Richard Pedersen	PEDERSEN13	6078

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EXAMINER	
TONGUE, LAKIA J	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,068	PEDERSEN ET AL.	
	Examiner	Art Unit	
	LAKIA J. TONGUE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 30* is/are pending in the application.

4a) Of the above claim(s) *27 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-26, in the reply filed on September 18, 2008 is acknowledged.

Applicant argues that:

1) Stephen et al. do not disclose synthetically glycosylated immunoglobulins.

2) Stephen et al. has not solved the problem of Gram negative bacteria being inaccessible to lysozyme due to the lipopolysaccharide layer in the bacterial cell wall.

3) The half-life of the immunoglobulins of Stephan et al. has not been prolonged.

Applicant's arguments have been fully considered and are deemed non-persuasive.

With regard to Point 1, the special technical feature has been identified as lysozyme and immunoglobulins. Stephan et al. (U.S. Patent 4,734,279) disclose a composition comprising lysozyme and immunoglobulins IgG, IgM, and IgA (see abstract). Moreover, Rudd et al. disclose that in the humoral immune system, all of the immunoglobulins are glycosylated (see abstract). Consequently, Stephan et al. inherently disclose glycosylated immunoglobulins.

With regard to Point 2, the claims are drawn to a composition, it is not necessary for Stephen et al. to solve the problem of Gram negative bacteria being inaccessible to lysozyme due to the lipopolysaccharide layer in the bacterial cell wall because the limitation is not recited in the rejected claim(s).

With regard to Point 3, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the half-life of the immunoglobulin has not been prolonged) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-27 and 30 are pending. Claim 30 has been withdrawn from further consideration as being drawn to non-elected inventions. Claims 28-29 have been canceled. Claims 1-26 are currently under examination.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on May 15, 2006 is in compliance with the provisions of 37 CFR 1.97 and has been considered. An initialed copy is attached hereto.

Claim Objections

3. Claim 20 is objected to because of the following informalities: 'monosachharide' should be spelled 'monosaccharide'. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to an antimicrobial composition comprising lysozyme and glycosylated immunoglobulins, wherein said glycosylated immunoglobulins have been produced by being dissolved in a solution comprising disaccharide or monosaccharide, wherein the glycosylated immunoglobulins are intact and/or resistant to proteases such as bacterial proteases and/or pancreatic proteases or lack the ability to fix complement.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession of the claimed

invention. To adequately describe the genus of glycosylated immunoglobulins, Applicant must adequately describe which immunoglobulins are resistant to proteases, proteolytic enzymes and/or resistant to acidic conditions or lack the ability to fix complement.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al. (Science, 1990, 257:1306-1310) disclose that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (see column 1, page 1306). Bowie et al. further disclose that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (see column 2, page 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al. (J. of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the

protein and by Lazar et al. (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, given not only the teachings of Bowie et al., Lazar et al. and Burgess et al. but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function the claimed proteins could not be predicted. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure

The specification does not disclose distinguishing and identifying features of a representative number of members of the genus to which the claims are drawn, such as what monosaccharide and disaccharides will confer resistance to proteases for a given antibody so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus.

A representative number of species means that the species that are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical

and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the claimed genus.

See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.
The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual

reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed. Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the Applicant had possession of the claimed invention at the time the instant application was filed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 12-15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12 and 13 are rendered vague and indefinite by the use of the phrase "wherein the glycosylated immunoglobulins are intact and/or resistant to proteases such as bacterial proteases and/or pancreatic proteases". It is unclear what is meant by said phrase, as it is not explicitly defined in the specification. What constitutes "immunoglobulins are intact and/or resistant to proteases such as bacterial proteases and/or pancreatic proteases"? Does the "and/or pancreatic proteases" further define the immunoglobulin or the proteases? As written, it is impossible to determine the

metes and bounds of the claimed invention.

Claim 15 is rendered vague and indefinite by the use of the phrase "immunoglobulins have lost their ability of complement fixation". It is unclear what is meant by said phrase, as it is not explicitly defined in the specification. What constitutes "having lost their ability"? When does one know that an immunoglobulin has lost its ability for complement fixation? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-14 and 16-26 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Stephan et al. (U.S. Patent 4, 734,279) as evidenced by Rudd et al. (Science, 2001; 291: 2370-2376) and Shu et al. (Nahrung, 1998; 42(2): 68-70).

The rejected claims are drawn to an antimicrobial composition comprising lysozyme and glycosylated immunoglobulins have been produced by being dissolved in a solution comprising disaccharide or monosaccharide.

Stephan et al. disclose a composition comprising a lysozyme and an immunoenhancing amount of immunoglobulins IgG, IgM and IgA (see abstract; column 1, lines 10-20). Stephan et al. disclose that mice were infected with *Pseudomonas aeruginosa* and the animals were protected by the administration of the immunoglobulin preparation (see column 2, lines 35-44). Stephan et al. disclose that the composition can be incorporated into a vehicle, such as tablets or ointments. Moreover, Rudd et al. which disclose that in the humoral immune system all of the immunoglobulins and most of the complement components are glycosylated (see abstract).

Stephan et al. do not specifically disclose that the immunoglobulins have affinity to Gram positive bacteria, viruses or antigen determinants on the cell wall of Gram negative bacteria. Moreover, Stephan et al. do not specifically disclose that the lysozyme is conjugated to a monosaccharide.

Shu et al. disclose that polysaccharide chain attachment, which includes monosaccharides such as mannose, to lysozyme is critical for excellent emulsifying properties (see abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Stephan et al. with regard to immunoglobulins having affinity to Gram positive bacteria, viruses or antigen determinants on the cell wall of Gram negative bacteria because the substitution of one known element for another

would have yielded predictable results to one of ordinary skill in the are at the time of the invention. Moreover, with regard to lysozyme conjugated to monosaccharide, "it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980).

With regard to claims 1, 16-18 and 22, it should be remembered that the products of the prior art reference appear to be the same as the product claimed by the applicant because they appear to possess the same or similar functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when the process does not change properties of the product in an unexpected manner. See *In re* Thorpe, 227 USPTO 964 (CAFC 1985); *In re* Marosi, 218 USPTO 289, 29222-293 (CAFC 1983); *In re* Brown, 173 USPTO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, great stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts to applicants product in order to overcome the aspect of the product's purity.

With regard to claim 2, claim limitations such as "for local use on mucosal membranes and/or skin" are being viewed as limitations of intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the art. See *In re Casey,* 152 USPQ 235 (CCPA 1967) and *In re Otto,* 136 USPQ 458, 458.

With regard to claims 23-26, limitations such as the form of the composition and the range of the lysozyme and glycosylated immunoglobulins are being viewed as limitations of optimizing experimental parameters.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT
10/30/08

/Robert A. Zeman/
for Lakia J. Tongue, Examiner of Art Unit 1645
November 10, 2008